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Claire C. Yotts

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants    SUEISHI et al.                      Art Unit:            Not Yet Assigned

Serial No.:    10/549,474                                  Examiner:           Not Yet Assigned

Filed:           September 14, 2005                      Customer No.:    21559

Title:           METHODS OF TREATING INFLAMMATORY DISEASES  
ASSOCIATED WITH BONE DESTRUCTION (As Amended)

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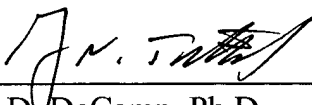
SUBMISSION OF TRANSLATION OF  
INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

Applicants submit herewith the Translation of the International Preliminary Report on Patentability corresponding to the above-referenced application. Applicants petition for any necessary extensions of time for submission of this document.

In addition, if there are any charges, or any credits, please apply them to Deposit  
Account No. 03-2095.

Respectfully submitted,

Date: 19 April 2006

  
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**Translation**

**PATENT COOPERATION TREATY**

**PCT**

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>D3-A0206P</b>	<b>FOR FURTHER ACTION</b>	See Form PCT/IPEA/416
International application No. <b>PCT/JP2004/002887</b>	International filing date (day/month/year) <b>05.03.2004</b>	Priority date (day/month/year) <b>19.03.2003</b>
International Patent Classification (IPC) or national classification and IPC		
Applicant <b>DNAVEC RESEARCH INC.</b>		

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>7</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input checked="" type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>	
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>	

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/002887

## Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on translations from the original language into the following language \_\_\_\_\_ which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
  - ☐ publication of the international application (Rule 12.4)
  - ☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☒ the international application as originally filed/furnished
- ☐ the description:
- pages \_\_\_\_\_ as originally filed/furnished
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ the claims:
- nos. \_\_\_\_\_ as originally filed/furnished
- nos.\* \_\_\_\_\_ as amended (together with any statement) under Article 19
- nos.\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- nos.\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ the drawings:
- sheets \_\_\_\_\_ as originally filed/furnished
- sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/002887

Box No. III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 1-5

because:

☒ the said international application, or the said claims Nos. 1-5

relate to the following subject matter which does not require an international preliminary examination (*specify*):

Claims 1-5 pertain to methods for treatment of the human body by therapy or surgery.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 1-5 are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. \_\_\_\_\_

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐

has not been furnished

☐

does not comply with the standard

the computer readable form

☐

has not been furnished

☐

does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/002887

**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

## 1. Statement

Novelty (N)	Claims	6-10	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	6-10	NO
Industrial applicability (IA)	Claims	6-10	YES
	Claims		NO

## 2. Citations and explanations (Rule 70.7)

## Citations

1. JP 2002-500623 A (The Board of Trustees of the Leland Stanford Junior University), 8 January 2002
2. JP 2000-229883 A (Chemo-Sero Therapeutic Research Institute), 22 August 2000
3. Journal of Immunology, 2002, Vol. 168, No. 1, pages 450-457
4. JP 07-265079 A (Yeda Research and Development Co., Ltd.), 17 October 1995
5. J. Biol. Chem., (2002), Vol. 277, No. 5, pages 3195-3201
6. JP 2003-503313 A (AU, Jessie L.S.), 28 January 2003
7. Nature, (2001), Vol. 412, No. 9, pages 647-651

## Explanations

Claims 6-8 and 10

The inventions set forth in claims 6-8 and 10 are not disclosed in any of the documents cited in the international search report and are, therefore, novel. However, these inventions do not involve an inventive step in the light of documents 1-3 cited in the international search report.

Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

Document 1 discloses a gene therapy composition that utilises a vector for expressing sprouty 2 protein and indicates that conditions that block angiogenesis, such as rheumatoid arthritis, are the kind of conditions to which this composition can be usefully applied.

Therefore, it would be obvious to a person skilled in the art to essentially apply a vector expressing sprouty 2 protein in the treatment of conditions such as rheumatoid arthritis.

Document 2 discloses a therapeutic agent for the treatment of chronic rheumatoid arthritis having bFGF (FGF2) antagonist as the active ingredient. Moreover, document 3 indicates that in model rats for rheumatoid arthritis, FGF2 promotes neoangiogenesis and neogenesis of osteoclasts, making the symptoms of arthritis deteriorate, and indicates that FGF2 promotes neogenesis of osteoclasts through FGF receptors (1). Furthermore, document 3 suggests that the neutralisation or control of FGF2 is effective in the treatment of rheumatoid arthritis.

Consequently, it would be easy for a person skilled in the art to conceive of selecting a protein or nucleic acid as a substances to block the effects of FGF2, to investigate its therapeutic activity in the treatment of disorders such as rheumatoid arthritis, and to apply it to a method wherein a vector that expresses said protein or nucleic acid is administered.

Claim 9

The invention set forth in claim 9 is not disclosed in any of the documents cited in the international search report and is, therefore, novel. However, the invention

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/002887

Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

does not involve an inventive step in the light of documents 1-7 cited in the international search report.

Document 1 discloses a gene therapy composition that utilises a vector for expressing sprouty 2 protein and indicates that conditions that block angiogenesis, such as rheumatoid arthritis, are the kind of conditions to which this composition can be usefully applied. Therefore, it would be obvious to a person skilled in the art to essentially apply a vector expressing sprouty 2 protein in the treatment of conditions such as rheumatoid arthritis.

Document 2 discloses a therapeutic agent for the treatment of chronic rheumatoid arthritis having bFGF (FGF2) antagonist as the active ingredient. Moreover, document 3 indicates that in model rats for rheumatoid arthritis, FGF2 promotes neoangiogenesis and neogenesis of osteoclasts, making the symptoms of arthritis deteriorate, and indicates that FGF2 promotes neogenesis of osteoclasts through FGF receptors (1). Furthermore, soluble FGF receptors, sprouty and spread proteins are known as substances that neutralise or control the effects of FGF2, as disclosed in documents 4-7. Therefore, it would be easy for a person skilled in the art to investigate the therapeutic activity of these proteins in the treatment of disorders such as rheumatoid arthritis, and to apply them to a method wherein a vector that expresses these proteins is administered.



**Box No. VIII** Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 6-8 and 10 pertain to a therapeutic composition for inflammatory diseases associated with bone destruction, such as rheumatoid arthritis having as the active ingredient a vector that codes for a protein or nucleic acid defined by its desired characteristics of "blocking signal transmission through fibroblast growth factor -2 (FGF2)-FGF receptor 1-Ras-Raf-MAP kinase". Of those proteins and nucleic acids having the aforementioned characteristics, only a small proportion are supported by the description in the sense defined in PCT Article 6 and/or can be regarded as having been disclosed in the sense defined in PCT Article 5.

Even taking into consideration the technical knowledge at the time of filing, it is impossible to define the scope of a protein or nucleic acid having such a characteristic as "a protein or nucleic acid for blocking signal transmission through fibroblast growth factor -2 (FGF2)-FGF receptor 1-Ras-Raf-MAP kinase."

Consequently, an opinion has been given concerning the relationship between the blocking of signal transmission (FGF2)-FGF receptor 1-Ras-Raf-MAP kinase and inflammatory diseases associated with bone destruction, and concerning a therapeutic composition for inflammatory diseases associated with bone destruction having as the active ingredient a vector that codes for a protein set forth in claim 9.